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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) Perez et al.	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on _____ Signature _____ Typed or printed name _____	Application Number 10/048,185	Filed June 17, 2002	
	First Named Inventor Perez et al.		
	Art Unit 1638	Examiner Robinson, Keith O'Neal	
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p> <p>I am the</p> <div style="display: flex; justify-content: space-between;"><div style="width: 45%;"><p><input type="checkbox"/> applicant/inventor.</p><p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p><p><input checked="" type="checkbox"/> attorney or agent of record. 53,202 Registration number _____</p><p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____</p></div><div style="width: 50%; text-align: center;"> _____ Signature Steven P. Lendaris _____ Typed or printed name (212) 408-2500 _____ Telephone number August 8, 2007 _____ Date</div></div> <p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p>			
<input type="checkbox"/> *Total of <u>1</u> forms are submitted.			

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Pre-Appeal Brief Request for Review

In response to the Official Action dated 5/30/07, Applicants respectfully request review of the pending final rejection. This request is being filed along with a Notice of Appeal and the appropriate Appeal Fee. No amendments are being filed with this request.

The Pending Claims

18. A method for producing an isotransgenic maize line comprising:

a) transforming cells of a hybrid plant, the parental lines of which are a maize line of interest that is recalcitrant or unsuited to transformation and has a transformation efficiency of zero to 1/100 and a maize line suited to transformation, with a vector comprising a T-DNA containing a transgene in order to obtain hybrid primary transformants, wherein said maize line suited to transformation is chosen from the group consisting of A188 and Hi-11 maize lines;

b) selecting for at least one individual among said hybrid primary transformants which has said T-DNA integrated only into the genome of said line of interest, in order to obtain selected individual(s), wherein said selection is performed by isolation and identification of genomic sequences of the host adjacent to the T-DNA;

c) backcrossing the individual(s) selected in step b) with an individual of said parental maize line of interest; and

d) selecting at least one transgenic individual obtained from the backcross in step c;

e) repeating steps c and d until said isotransgenic maize line is produced.

23. The method of Claim 18 further comprising crossing said isotransgenic maize line obtained in step e) and a second line of interest.

24. The method of Claim 18, wherein said transgene encodes a protein which confers agronomic properties and/or properties of resistance to diseases.

25. The method of Claim 18, wherein said line of interest is a commercial elite line.

27. The method of Claim 23, wherein the second line of interest is an isotransgenic plant line.

The Pending Rejections

There are two pending rejections in the instant application: (1) Claims 18, 23-25, and 27 stand finally rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ishida et al., Nature Biotech. 14:745-750 (1996) ("Ishida"), in view of Does et al., Plant Mol. Biol. 17:151-153 (1991) ("Does"), Hiei et al., Plant J., 6(2):271-282 (1994) ("Hiei"), Armstrong et al., Theor. Appl. Genet. 84: 755-762, (1992) ("Armstrong"), and Ragot et al., Techniques et utilisations des

Marqueurs moléculaires 45-56 (1994) (“Ragot”); and **(2)** Claims 18, 23-25, and 27 stand finally rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Lundquist et al., US Patent No. 5,508,468 (“Lundquist”), in view of Chyi et al., Mol. Gen. Genet. 204:64-69 (1986) (“Chyi”).

The Examiner Has Not Established A *Prima Facie* Case of Obviousness

(1) Over Ishida, Does, Hiei, Armstrong, and Ragot

The Examiner’s basis for rejecting the pending claims as unpatentable over Ishida, Does, Hiei, Armstrong, and Ragot is included in the 6/25/04 Office Action¹, and is detailed at pages 4-6 of the Applicants’ Response of 3/13/07. In brief, the Examiner contends that Ishida teaches a method for transforming hybrid maize plants using plants identical to those employed in the claimed method. However, the Examiner concedes that Ishida does not teach **(1)** the selection of hybrid primary transformants having integrated T-DNA, **(2)** the back-crossing of selected hybrid primary transformants with the parental line of interest, and **(3)** the selection of at least one transgenic individual derived from each backcrossing until an isotransgenic line is produced. Given the deficiencies of Ishida, the Examiner attempts to combine that reference with Does and Hiei, both of which describe assays for identifying T-DNA integration, along with the RFLP analysis and backcrossing methods for maize described in Armstrong. The Examiner contends that one of skill in the art would be motivated to make such a combination given on the desirability of isogenic transgenic maize lines and success in obtaining them taught by Ragot. As pointed out in the previously-filed Responses, Applicants respectfully disagree with the Examiner and reiterate that the cited references, taken singly or in combination, fail to teach or suggest a limitation of the claims which is crucial to the success of the invention and otherwise fail to establish *prima facie* obviousness.

Applicants respectfully submit that several steps that must be followed in order to properly establish an obviousness rejection under 35 U.S.C. § 103.² First, the scope and content of the prior art are to be determined, then any differences between the prior art and the claims at issue are to be ascertained, and finally the level of ordinary skill in the pertinent art is resolved. It is against this background that the obviousness or nonobviousness of the subject matter is determined by identifying whether one of ordinary skill in the art would have a reasonable

¹ In each of the prior Office Actions the Examiner cites either directly or indirectly (i.e., through a chain of Office Actions) to the Office Action of 6/25/04 as providing the foundation for this rejection under §103(a).

² *Graham v. J. Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966),

expectation of success in achieving the claimed invention by making the proposed combination.³ Applicants also note that the Federal Circuit has clearly stated that there can be no suggestion or motivation to combine a group of references if the proposed combination would render the subject matter disclosed in those references unsatisfactory for their intended purpose.⁴

Applicants have discussed the scope and content of the cited art at length in the Responses filed 3/13/07 (see pages 7-10), 9/14/06 (see pages 6-9), 3/20/06 (see pages 13-16); 6/21/05 (see pages 14-15 and the associated Declaration of Pascual Perez), 3/21/05 (see pages 12-14), and 10/21/04 (see pages 22-24). In the interest of brevity, we will not repeat that analysis but instead focus on the differences between the cited art and the claims at issue.

First, Applicants submit that the Examiner has not established that the cited art teaches or suggests the selection step “(b)” of Claim 18. This step identifies the presence of the transgene and selects only for those plants where the transgene has integrated into a chromosome of the line of interest. In the absence of this selection step, it would be impossible to predict that the subsequent backcrosses would generate an isotransgenic maize line as claimed. Initially the Examiner attempted to counter Applicant’s position by contending that Does teaches such a selection method⁵, however in the Office Action of 5/30/07, the Examiner concedes that Does fails to teach such a selection method and instead argues, based solely on the teachings of the instant specification, that Does could be modified to achieve the claimed selection step.⁶ As the Examiner is aware, such a hindsight reconstruction based solely on the Applicants’ specification is improper. For example, pages 6-7 of the instant Office Action, point out that “so long [as a judgment on obviousness] takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, **and does not include knowledge gleaned only from the applicant’s disclosure**, such a reconstruction is proper.”⁷

The Examiner also maintains that how the selection step is performed “does not affect the principle component of the claimed step, which is selecting for at least one individual which has T-DNA integrated into the genome of interest.”⁸ However, the Examiner ignores the fact that the system described in Does (which identifies T-DNA only after it has been excised from

³ M.P.E.P. §2143; *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)

⁴ See, *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984); *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)

⁵ See Office Action of 6/25/04, pages 16-17.

⁶ See Office Action of 5/30/07, pages 2-3.

⁷ See Office Action of 5/30/07, page 6-7 (emphasis added).

⁸ See, Office Action of 5/30/07, page 3

genomic DNA) cannot differentiate in which line the T-DNA had been integrated, and therefore cannot be used to select for integration of the transgene into the line of interest. That the Examiner can point to alternative methods of performing the step disclosed in the instant specification⁹ does not alter the fact that the method described in Does is incapable of achieving that principle component. Given the deficiency of Does, and the failure of any of the other pieces of art to supply the missing teaching, Applicants respectfully assert that the cited art fails to teach or suggest all of the claim limitations, therefore a *prima facie* case of obviousness has not been established.

Applicants further note that the Examiner has proposed to combine the teaching of Does with the teachings of Ishida and Hiei. However, such a modification of Does would both render it unsatisfactory for its intended purpose and change its principle of operation. Specifically, the method described in Does relies on the ability of a *single* inserted T-DNA containing construct to be excised and circularized by ligation followed by digestion by a restriction enzyme and inverse PCR. In contrast, both Ishida and Hiei rely on the use of a super binary vector that is comprised of *two different plasmids*, where each construct includes T-DNA regions.¹⁰ In order to modify Does to accommodate the presence of the second T-DNA containing plasmid, its principle of operation would necessarily have to be changed. Furthermore, the stated aim of Does, would be frustrated by any such modification.¹¹ The Examiner's rebuttal that the cited references are in an analogous fields is irrelevant to the instant issue, i.e. that the cited references cannot be functionally combined to achieve the claimed invention. In light of the foregoing, Applicants respectfully submit that the Examiner has failed to identify some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine references' teachings and therefore a *prima facie* case of obviousness has not been established.

(2) Over Lundquist and Chyi

The Examiner's basis for rejecting the pending claims as unpatentable over Lundquist and Chyi can be found at pages 6-7 of the 12/13/06 Office Action. In brief, the Examiner contends that one of ordinary skill in the art would have been motivated to combine the RFLP

⁹ See, Office Action of 5/30/07, page 3

¹⁰ See, Ishida page 749 and Hiei page 272

¹¹ See, Does, Abstract "Our aim was to obtain transgenic tobacco plants containing one integrated T-DNA copy per genome."

analysis and backcrossing of tomatoes taught by Chyi with the method of producing transgenic maize via microparticle bombardment taught by Lundquist. As pointed out in the Response of 3/13/07, Applicants submit that the cited references, taken singly or in combination, fail to establish *prima facie* obviousness.

Without repeating in full the arguments presented at pages 10-13 of the 3/13/07 Response, Applicants respectfully point out that the Examiner has improperly used hindsight to reconstruct the claimed invention using the Applicants' disclosure as a blueprint. Specifically, Applicants point out that the Examiner has cherry-picked references that have no relation to the instant invention but that disclose general ideas related to recombinant DNA technology. For example, the Examiner attempts to combine Lundquist with Chyi, however, success or failure of a transformation system designed for tomato plants, as disclosed in Chyi, is wholly distinct from the currently claimed transformation of maize.¹² Accordingly, Applicants respectfully submit that neither Lundquist or Chyi provide motivation to combine their respective teachings, and neither singly nor taken together, teach or suggest the presently claimed invention.

Applicants also note that Lundquist and Chyi, either alone or in combination, do not teach or suggest the selection step "(b)" of Claim 18. The Examiner contends that Chyi teaches such a selection method, asserting that the cited reference teaches "using RFLPs to identify genomic sequences of the host adjacent to the T-DNA in tomato and backcrossing individuals to parental lines."¹³ However, the Examiner has not identified a means taught or suggested by Chyi to select a specific individual among the hybrid primary transformants, wherein the specific individual contains the T-DNA integrated within a chromosome originating from the line of interest as required by the claim. Without this step, as discussed above, it would be impossible to predict that the subsequent backcrosses would generate an isotransgenic maize line. Given the deficiency in the Examiner's position, Applicants respectfully assert that the cited art fails to teach or suggest all of the claim limitations, and therefore a *prima facie* case of obviousness has not been established.

¹² See Office Action of 3/13/07, pages 11-12. Applicants note that this combination also contradicts the Examiner's earlier position that such methods cannot be extrapolated across species. See Office Action of 1/21/05, page 4.

¹³ See, Office Action of 12/13/06, page 6, citation removed.